REMARKS

Applicants have amended their claims in order to further clarify the definition of various aspects of the present invention. Specifically, applicants have amended claim 1 to recite that the saccharides, of which the core material is made, comprise granulated sugar or lactose. Note, for example, the paragraph bridging pages 11 and 12 of applicants' specification. In light of amendments to claim 1, claim 2 has been canceled without prejudice or disclaimer. In addition, applicants have amended claim 5 to insert a comma between "amylase" and "protease".

The rejection of claims 5-9 under the second paragraph of 35 USC §112, set forth on page 2 of the Office Action dated July 10, 2007, is noted. As indicated by the Examiner, claim 5 contained a typographical error, and as understood by the Examiner, "amylase" and "protease" are separate materials, and are now separated by a comma. In light of the present amendment of claim 5, it is respectfully submitted that the rejection of claims 5-9 under the second paragraph of 35 USC §112 has been overcome.

Applicants are adding new claims 23-25 to the application. Claim 23, dependent on claim 1 recites that the bioactive ingredient is suspended in the hardened oil, forming a mixture of hardened oil and bioactive ingredient, with this mixture forming the layer that covers the core material. Claim 24, dependent on claim 1, recites that the core material consists of the granulated sugar or lactose; and claim 25, also dependent on claim 1, recites that the core material is free of bioactive ingredient. Note, for example, the first full paragraph on page 8 of applicants' specification. Note also the paragraph bridging pages 10 and 11 of applicants' specification; see, further, the last full paragraph on page 12 of applicants' specification.

Applicants respectfully submit that all the claims presented for consideration by the Examiner on the merits in the above-identified application patentably distinguish over the teachings of the references applied by the Examiner in rejecting claims in the Office Action dated July 10, 2007, that is, the teachings of the U.S. Patents to Shibahara et al, No. 5,753,223, to Nishimura, et al, No. 5,571,527, and to Ludwig et al, No. 4,293,539, even with support from Answers.com, under the provisions of 35 USC §102 and 35 USC §103.

It is respectfully submitted that these references as applied by the Examiner would have neither taught nor would have suggested such a granular composition as in the present claims, having a core material and a layer covering the core material, the core material made of saccharides comprising granulated sugar or lactose, and with the layer that covers the core material being made of a hardened oil and a bioactive ingredient. See Claim 1.

More specifically, it is respectfully submitted that the applied references would have neither taught nor suggested such granular composition, having such core material and such layer covering the core material, and wherein the core material consists of the granulated sugar or lactose (see claim 24), or wherein the core material is free of bioactive ingredient (see claim 25).

Moreover, it is respectfully submitted that these applied references would have neither taught nor would have suggested such granular composition as in the present claims, having features as set forth in claim 1, and, moreover, wherein the bioactive ingredient is suspended in the hardened oil, forming a mixture of hardened oil and bioactive ingredient, with this mixture forming the layer that covers the core material. See claim 23.

In addition, it is respectfully submitted that these applied references would have neither taught nor would have suggested such granular composition as in the

present claims, having features as discussed previously in connection with claim 1, and, moreover, wherein the hardened oil comprises a hardened palm oil. See claim 3.

Furthermore, it is respectfully submitted that these references would have neither taught nor would have suggested such granular composition as in the present claims, having features as discussed previously in connection with claim 1, and, moreover, wherein the bioactive ingredient comprises an enzyme (see claim 4), more specifically, an enzyme as in any one of claims 5-9; and/or wherein the bioactive ingredient comprises an antibiotic (see claim 10), more specifically, colistin (see claim 11); and/or content of bioactive ingredient, as in claim 12.

The invention as presently being considered on the merits in the above-identified application is directed to a granular composition containing a bioactive ingredient. The composition has enhanced wet-heat stability. As to what is meant by wet-heat stability, note the second full paragraph on page 8 of applicants' specification.

Bioactive ingredients, such as enzymes, antibiotics, vaccines, etc., are generally in the form of powders in a dry state; and, under such condition, the bioactive ingredients are used in pharmaceutical preparations, foods, detergents, feed for domestic animals, etc. However, such bioactive ingredients, in the form of powders, have disadvantages, because of their poor fluidity and dusting characteristics. Moreover, when the bioactive ingredients are added to feed for domestic animals, activities of the ingredients generally decrease at high temperature and high humidity.

In view of the foregoing, it has been demanded to provide stable bioactive ingredient-containing preparations, such as pharmaceutical preparations, avoiding

disadvantages of prior materials, and wherein the activity does not drastically decrease at high temperatures and high humidity.

Various proposals for providing preparations avoiding the above-discussed problems have been made, as discussed on pages 2 and 3 of applicants' specification. However, these proposals have disadvantages in that stability of the bioactive ingredient at high temperatures and high humidity is low, and/or a complicated production process, which takes a long time and unique machines, is required.

Against this background, applicants provide a granular composition stable at high temperature and high humidity, and which can be used with various bioactive ingredients, e.g., in powder form. Applicants have found that a structure in which wet-heat does not directly affect the bioactive ingredient can be obtained by utilizing the fact that fats have the properties of being molten and solidified at predetermined temperatures, and by suspending bulk powder of the bioactive ingredient in the fats to allow the bulk powder to adhere to an appropriate carrier, e.g., formed into a film on the carrier. The presently claimed granular composition can be formed by a relative simple process, utilizing simple apparatus. See the first full paragraph on page 4 of applicants' specification. Note also the paragraph bridging pages 38 and 39 of applicants' specification.

That the present invention achieves advantageous results in maintaining high activity of the bioactive ingredient, even after wet-heat treatment, can be seen in the Examples and comparison examples in the present invention, starting on page 15 of applicants' specification. In particular, note Table 1 on page 33 of applicants' specification. It is respectfully submitted that this shows unexpectedly better maintenance of enzyme activity after wet-heat treatment, for the present invention, as compared to powdery compositions.

Shibahara et al discloses a feed additive composition for ruminant animals, in which biologically active substances are coated with a coating composition which is stable in a first stomach (rumen) of a ruminant animal and which releases the biologically active substances in the animal's post-abomasum digestive organs, thereby permitting digestion and absorption of the biologically active substances in the post-abomasum digestive organs. Note, column 1, lines 11-20. This patent discloses that the composition is prepared by coating a core containing one or more biologically active substances with at least one protective substance selected from the group consisting of hardened vegetable fats and oils, hardened animal fats and oils, fatty acid esters and phospholipids, where the coating contains an enzyme which hydrolyzes the protective coating substance itself and/or an enzyme activator which activates an enzyme secreted from the post-abomasum digestive organs of the ruminant, which secreted enzyme hydrolyzes the protective coating substance. Note column 2, lines 47 – 61. See also column 4, lines 10-12. This patent further discloses that the outermost surface portion of the coating layer contains substantially no enzyme. Note column 3, lines 1-15. As for the biologically active substances, note column 3, lines 24-45. See also column 5, lines 5-10.

It is emphasized that Shibahara et al discloses that the core material contains a biologically active substance. It is respectfully submitted that this patent would have neither taught nor would have suggested, and in fact would have taught away from, the granular composition as in the present claims, wherein the core material is made of saccharides, the saccharides comprising granulated sugar or lactose, as in claim 1; and/or more specifically, wherein the core material consists of the granulated sugar or lactose, and/or the core material is free of bioactive ingredient (see claims 23 and 25).

Specifically, note that according to Shibahara et al, the bioactive material for the ruminant is contained in the core material, and the enzyme contained in the coating layer is used for accelerated degradation of the protective surface layer, in the post-abomasum digestive organs of the ruminant animal, with release of biologically active substance that is contained in the core (the protective surface layer acting to protect the core material in the rumen). This can be seen in the description in Shibaraha et al that the outermost surface portion of the coating layer contains substantially no enzymes, to prevent the coating layer from being degraded by avoiding contact of the enzyme with a digestive fluid.

In contrast, according to the present invention, the core material is saccharides which comprise granulated sugar or lactose; the core material does not contain biologically active substances, the biologically active substances being contained in the cover layer with the hardened oil. According to the present invention, having the cover layer and core material, a composition which is stable under conditions of high temperature and high humidity at the time of production is achieved.

Thus, as can be seen in the foregoing, the composition and function of the present invention is different from that of Shibahara et al; and it is respectfully submitted that the material of Shibahara et al would have neither taught nor would have suggested the present invention.

It is respectfully submitted that the additional teachings of the secondary applied references, Nishimura et al and Ludwig et al, as applied by the Examiner, would not have rectified the deficiencies of Shibahara et al, such that the presently claimed invention as a whole would have been obvious to one of ordinary skill in the art.

Nishimura et al discloses a granular agent for ruminants, comprising a core granular agent containing a physiologically active substance coated with a coating layer comprising (a) a first coating material composed of one or more substances selected from the group consisting of a fatty acid having 12 to 22 carbon atoms or ester thereof, an animal or vegetable fat and fatty oil or a hardened animal or vegetable fat and fatty oil, having a specified melting point, and a wax having a specified melting point and (b) a second coating material composed of tabular crystals of a substance which is sparingly water-soluble under a neutral condition but is readily water-soluble under an acid condition, the coating layer having a laminar structure in which the tabular crystals are arranged in a laminated state, the coating materials and coating layer being further defined. See column 3, line 50, through column 4, line 2. Note also column 5, lines 1-19.

Even assuming, *arguendo*, that the teachings of Nishimura et al were properly combinable with the teachings of Shibahara et al, such combined teachings would have neither disclosed nor would have suggested such granular composition as the present claims, including the core material made of saccharides comprising granulated sugar or lactose, with the bioactive ingredient included in the layer that covers the core material, more specifically, wherein the core material consists of the granulated sugar or lactose and/or wherein the core material is free of bioactive ingredient.

Ludwig et al discloses formulations capable of supplying an effective dose of a drug to an animal over a prolonged period of time, comprising an effective amount of active ingredient and pharmaceutically acceptable diluents and carriers therefor, intermittently dispersed throughout a copolymer derived from about 60-95 weight per cent lactic acid and about 40-45 weight per cent glycolic acid, the copolymer being

further defined. Note column 1, line 67 through column 2, line 12. See also column 2, lines 52-57; and column 4, lines 18-21.

Even assuming, *arguendo*, that the teachings of Ludwig et al were properly combinable with the teachings of Shibahara et al, as applied by the Examiner, such combined teachings would have neither disclosed nor would have suggested the present invention, including the core material made of saccharides comprising granular sugar or lactose, with the layer that covers the core material being made of a hardened oil and the bioactive ingredient, in particular, wherein the core material consists of the granulated sugar or lactose and/or wherein the core material is free of bioactive ingredient.

The contention by the Examiner on page 3 of the Office Action mailed July 10, 2007, that Shibahara et al teaches a granular composition wherein the core is "granulated sugar such as sucrose, glucose and starch" is noted. Shibahara et al discloses that the biologically active substance is provided in the core material. This patent discloses that these biologically active substances can include, *inter alia*, carbohydrates such as starch, sucrose and glucose. It is respectfully submitted that the Examiner errs in contending that Shibahara et al discloses that the core of the material can be granulated sugar; in this regard, it is respectfully submitted that Shibahara et al discloses active ingredients including various carbohydrates, and does not refer to lactose or granulated sugar. Contrary to the conclusion by the Examiner, it is respectfully submitted that Shibahara et al would have neither taught nor would have suggested the present invention.

Note that according to Shibahara et al, the disclosed enzymes in the coating are not in the outer surface coating, and are used for degrading the coating. Such disclosure would have taught away from the presently claimed subject matter, including the bioactive ingredient in the layer that covers the core material; and,

moreover, would have taught away from the composition as in the present claims including the core material made from saccharides comprising granulated sugar or lactose, and function thereof.

In view of the foregoing comments and amendments, reconsideration and allowance of all claims being considered on the merits in the above-identified application are respectfully requested.

Applicants request any shortage or excess in fees in connection with the filing of this paper, including extension of time fees, and for which no other form of payment is offered, be charged or credited to Deposit Account No. 01-2135 (Case No.: 1333.45033X00).

Respectfully submitted,
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